PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61M 5/145, B01F 13/08 — A1

(11) International Publication Number: **WO 00/12157**

(43) International Publication Date: 9 March 2000 (09.03.00)

(21) International Application Number: PCT/EP99/06289

(22) International Filing Date: 26 August 1999 (26.08.99)

(30) Priority Data:
198 40 536.7 28 August 1998 (28.08.98) DE

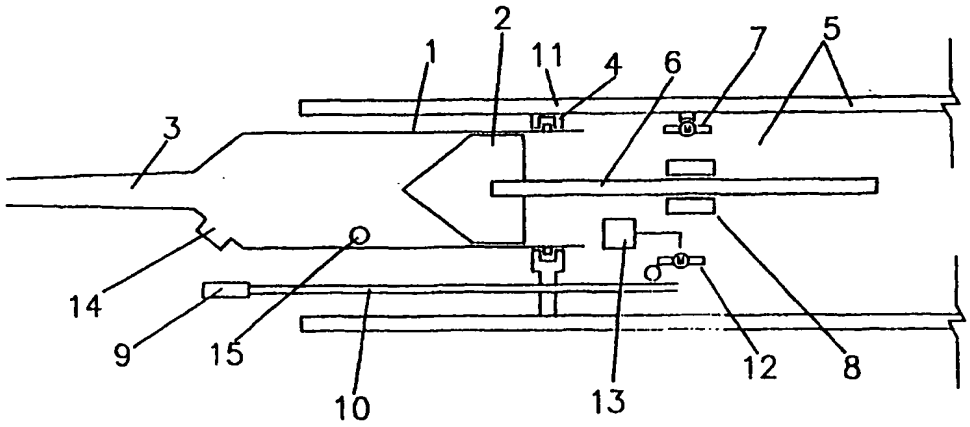
(71) Applicant *(for all designated States except US)*: SCHERING AKTIENGESELLSCHAFT [DE/DE]; Müllerstrasse 178, D–13353 Berlin (DE).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: URICH, Klaus [DE/DE]; Parkstrasse 27a, D–13129 Berlin (DE).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: SYRINGES AND INJECTORS INCORPORATING MAGNETIC FLUID AGITATION DEVICES



(57) Abstract

A syringe for use with an injector includes a body comprising a distal discharge end, a plunger movably disposed within the body, and an agitation element disposed within the body between the plunger and the distal discharge end. The agitation element is acted on by a magnetic field to agitate the contents of the syringe. The magnetic field is generated by a source operably associated with the syringe or the injector. Preferably, the syringe contains an ultrasound contrast agent that is agitated by the agitation element. An injector system and a method for agitating the contents of a syringe are also provided.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

SYRINGES AND INJECTORS INCORPORATING MAGNETIC FLUID AGITATION DEVICES

Background of the Invention

The present invention relates generally to movement devices for agitating the contents of syringes and, more particularly, to syringes and injectors incorporating movement devices for agitating contrast agents disposed within the syringes.

Syringes which are prefilled with ultrasound contrast agents are clamped into injectors for injection. The syringes remain therein for several minutes to one or more hours. The duration of one or more injections, including the intervening periods between the injections, may last for more than 10 minutes. Depending on the nature and composition of the contrast agent, dissociation commences at different times. During this period, the ultrasound contrast agent becomes dissociated and the phases are separated from one another. The ultrasound contrast agent as a whole is no longer homogeneous. In order to restore this homogeneity, the entire injector, including the syringe clamped therein, is moved manually. Movements of this nature are not reproducible, and sufficient homogenization is not ensured.

Ultrasound contrast agents are sensitive to transverse forces. Under excessively high forces, the particles are torn apart and destroyed. This impairs the quality of the ultrasound contrast agent. Thus, to maintain the suspension of particles in ultrasound contrast agents it is necessary to agitate the agents, but at the same time the particles must not be destroyed by the agitation.

Ultrasound contrast agents are generally described in Supplement to Diagnostic Imaging, May 1995, Advanced Ultrasound, Editor: Peter L. OGLE, Editorial Offices: 600 Harrison St. San Francisco, CA 94107 USA.

Glass syringes and plastic syringes are described extensively in the publication by Junga (M. JUNGA (1973) Pharm. Ind. Vol. 35, No. IIa, pages 824 to 829). A mixture of glass and plastic is described in PCT Publication No. WO 96/00098.

Injectors are generally described in EP Publication No. 0 584 531.

Summary of the Invention

The present invention provides apparatuses and methods for maintaining the homogeneity and integrity of an ultrasound contrast agent over a relatively long period of time without destroying the consistency of the ultrasound contrast agent and hence impairing its pharmacological and diagnostic properties. The dissociation begins immediately after the initial preparation of the ultrasound contrast agent, and at the latest after the syringe has been inserted into the injector when the latter is at rest (i.e., is not moving). By maintaining the homogeneity and integrity of the particles suspended in the contrast agent at optimal levels, the diagnostic properties of the contrast agent can be optimized.

The present invention further provides apparatuses and methods for continuous, controlled and/or reproducible agitation procedures for contrast agents. These procedures can be utilized between the time of preparation of the contrast agents and their injection into a patient.

Further, the present invention provides agitation procedures that can be specifically designed and/or adjusted for specific contrast agents, including ultrasound contrast agents.

Also, the agitation procedures may be designed to minimize turbulent agitation of the contrast agents, thereby reducing shear forces and other stresses that could be harmful to the integrity of the particles suspended in the contrast agents.

Moreover, the present invention provides a controlled application of magnetic energy to maintain the homogeneity of the contrast agent suspension, without mixing or otherwise destroying the particles of the contrast agents.

One aspect of the present invention is achieved by means of a syringe which is filled with ultrasound contrast agent for administering the contents thereof by means of an injector, wherein at least one ferromagnetic or magnetic agitation element is arranged in the syringe. The agitation element can be exposed to a magnetic field, the source of which is arranged in the syringe, on the syringe, around

the syringe. in the injector or associated with an accessory for the injector, and which is movable with respect to the syringe.

Another aspect of the present invention is achieved by means of an injector or an accessory associated with an Injector, which induces or is able to induce a magnetic field that acts on at least one ferromagnetic or magnetic agitation element in the syringe. The source of the magnetic field may be arranged in the syringe, on the syringe, around the syringe, in the injector or the accessory associated therewith. Further, the direction of the lines of flux in the magnetic field may be variable with respect to the syringe.

In one embodiment, the injector accommodates the syringes which are filled with an ultrasound contrast agent via at least one holder.

In a preferred embodiment, the present invention provides a combination of a syringe filled with a contrast agent and an injector or an accessory for use with an injector. At least one ferromagnetic or magnetic agitation element is contained in the syringe and is exposed to a magnetic field, the source of which is arranged in the syringe, on the syringe, around the syringe or in the injector or an accessory associated therewith. Further, the direction of the lines of flux of the magnetic field may be three-dimensionally variable with respect to the syringe.

In another embodiment, the injector may be connected to the syringe or the injector accessory may be connected to the syringe via the injector.

In another preferred embodiment, the syringes are made from plastic, glass or a plastic/glass material. Further, the syringes may be disposable syringes.

Moreover, the agitation element may be exposed to the magnetic field via a magnetic field coupling.

The present invention, along with further aspects and attendant advantages, will best be understood by reference to the following detailed description taken in conjunction with the accompanying drawings.

Brief Description of the Drawings

Figure 1 is an elevated, cross-sectional view of an injector system incorporating a movable magnet.

Figure 2 is an elevated, cross-sectional view of an injector system incorporating helically running magnetic conductors.

Figure 3 is a graphical view comparing the Doppler signal intensity of a contrast agent with resuspension versus that of the contrast agent with no resuspension.

Figure 4 is a graphical view comparing the Doppler signal intensity of a contrast agent with resuspension versus that of the contrast agent with no resuspension.

Figure 5 is a graphical view comparing the Doppler signal intensity of a contrast agent with no resuspension versus that of the contrast agent with low-speed and high-speed resuspensions.

Detailed Description of the Presently Preferred Embodiments

Before turning to a detailed description of the preferred embodiments, as illustrated in Figures 1 and 2, the present invention is described first below in general terms applicable to all suitable embodiments thereof.

As an initial matter, the terms "syringe" and/or "syringes" as used herein can mean and encompass the following terms and devices: cartridges (large-volume syringe with a volume of at least 100 ml); ampoule syringes; disposable syringes; disposable syringe ampoules; throw-away syringe ampoules; throw-away syringes; injection ampoules; disposable injection ampoules; ready-for-injection ampoules; cylindrical ampoules; twin-chamber injection ampoules; two-chamber syringes; two-chamber syringe ampoules; and no-delay syringes.

In addition, the terms "injector" and/or "injectors" as used herein can mean and encompass the following terms and devices: infusion pumps; infusers;

perfusors; and all other applicators or devices that operate to empty syringes of fluid contain therein.

Further, the terms "accessory" and/or "accessories" as used herein can mean and encompass the following: all devices which are or may be physically connected to an injector and operate to move the magnetic field in such a way that the agitation element in the syringe changes position. Typical accessories include collars, cylinders and attachments which act magnetically on the agitation element. The accessory fulfills the function of moving the agitation element by means of a magnetic force.

The magnetic field used with the present invention may preferably comprise an electromagnetic field. The electromagnetic field can be generated by means of a multiplicity of electromagnets which are arranged, for example, in the manner of a linear motor. The electromagnets may surround the syringe in the manner of a collar or sleeve. The electromagnets may also form part of the housing of the injector. The electromagnets are operable to attract an agitation element disposed within a syringe. The agitation element comprises at least one ferromagnetic or magnetic part. The arrangement of the electromagnets may be such that a linear, circular or helical movement of the agitation element, as well as mixed forms thereof, are possible.

In another embodiment, various coils can be arranged around the circumference of or within the cylinder or body of the syringe, with the current flowing through the coils at different times.

Further, the source of the magnetic field may be movably disposed outside of the syringe. In this case, the magnetic field source may comprise a magnet or a ferromagnetic element, the latter solution being possible when the agitation element is a permanent magnet.

Moreover, the magnetic field source may also be generated by means of electromagnets or coils that are situated in the wall of the syringe cylinder or body. In this embodiment, the electromagnets or coils are preferably controlled by the injector.

In the present invention, the agitation element may be encased by various substances. Suitable substances for the casing include, but are not limited to, glass and plastic materials, such as Teflon, which are preferably inert with respect to contrast agents. The use of a casing also reduces friction, which results in a reduction in or avoidance of particles within the syringe. Preferably, the agitation element is in the form of a ball.

The syringe preferably includes a recess therein for accommodating the agitation element. The recess preferably is designed in such a way that the agitation element can slide into or out of the recess. The recess preferably lies outside the movement range of the plunger in the syringe or itself forms part of the plunger.

Also, the recess may be formed both in the syringe and in the plunger. Preferably, the recess is positioned at or adjacent to the distal end (i.e., the syringe end having the needle attachment, hose attachment or luer lock fitting) of the syringe.

Further, the recess may be situated in the distal cover of the syringe cylinder or located in the syringe cylinder itself, close to the cover. In this case, a lock is preferably included to prevent the agitation element from blocking the syringe outlet.

In addition, the recess may comprise an annular recess that is disposed in the cover of the syringe cylinder. This design eliminates the need to orient the agitation element with respect to the syringe when the latter has been completely emptied.

Preferably, the recess is arranged in the syringe plunger. In this case, careful attention should be paid to the accurate orientation of the plunger with respect to the magnetic field source, unless an annular recess is situated in that part of the plunger which faces toward the needle attachment end (i.e., distal end) of the syringe.

An important feature of the syringe is the design of the plunger, the closure, and the corresponding distal opening. The syringes preferably are paramagnetic or diamagnetic.

The electromagnets and the mechanical control of the present invention should be configured in such a way that the force field (electromagnetic, magnetic or ferromagnetic) is active only in that region of the syringe which is filled with the contrast agent. For example, if the plunger moves in the distal (i.e., forward) direction, only those regions of the electromagnets which lie in the distal direction of the syringe with respect to the plunger may be activated. The intensity and frequency of the movement has to be controlled, in accordance with the sensitivity of the contrast agent and in accordance with the movement sequence, in such a way that the consistency of the particles in the ultrasound contrast agent is not adversely affected.

The agitation element should preferably be controlled in such a way that sufficient homogenization is ensured but the particles in the ultrasound contrast agent are not destroyed by transverse forces. Sensors that monitor the movement of the force field and preferably also of the plunger may be used in order to ensure optimum mixing.

Turning now to the drawings of the preferred embodiments, Figure 1 illustrates a syringe 1 having a plunger 2 disposed therein and a needle attachment end 3. The syringe 1 is connected to an injector 5 via a holder 4. The syringe 1 can be inserted into the holder 4 in a reversible manner.

The injector 5 comprises a ram 6 which is connected to the plunger 2 of the syringe 1. The ram 6 is moved with respect to the housing of the injector 5 by a motor 7, the motor turning a ring 8 which has a screw thread and surrounds the ram 6, which likewise has a complementary screw thread. The ring 8 is rotatable with respect to the housing.

A magnet 9, preferably a permanent magnet, can be moved with respect to the syringe 1 and a collar 11 by means of a linkage 10, the collar forming part of the injector 5. The collar 11 may also be attached to an injector 5 as an accessory. The linkage 10, which preferably comprises a toothed rack, is moved by a thrust motor 12, a pinion of which engages the toothed rack. The movement of the thrust motor 12 is controlled by a control device 13. In so doing, it is possible to take into account individually the nature of the contrast agent, the syringe size, the volume per minute of the injection and the stress on the patient.

At the distal end 3 of the syringe 1, the syringe 1 comprises a bulged recess 14 which is able to accommodate an agitation element 15. Preferably, the agitation element 15 is in the form of a ball. During an injection procedures, but before the syringe 1 is completely emptied of the fluid contained therein, the control system 13 operates to adjust the position of the ball 15 in such a way that the ball 15 can slide into the recess 14 to allow the plunger 2 to travel completely toward the needle attachment end or distal end 3 of the syringe to discharge the contents therefrom.

Figure 2 illustrates a syringe 1 having a plunger 2 disposed therein and a needle attachment end 3. The syringe 1 is connected to an injector 5 via a holder 4. The syringe 1 can be inserted into the holder 4 in a reversible manner. The injector 5 has a ram 6 which is connected to the plunger 2 of the syringe 1. The ram 6 is moved with respect to the housing of the injector 5 by a motor 7, the motor turning a ring 8 which has a screw thread and surrounds the ram 6, which likewise has a complementary screw thread. The ring 8 is rotatable with respect to the housing.

A multiplicity of coils 16, through which current preferably can flow separately from one another, surround the syringe in a magnetic collar 17, the magnetic collar forming part of the injector 5. The magnetic collar 17 may also be attached to an injector 5 as an accessory. The coils 16 are individually activated by a control unit 18, so that a magnetic field can continuously change its position with respect to the syringe 1.

The magnetic field moves an agitation element 15, which is preferably in the form of a ball, within the syringe 1. The plunger 2 comprises, at the end facing toward the needle attachment end 3, a recess 20 that is able to accommodate the ball 15. The control unit 18 is controlled by means of the control device 13. In so doing, it is possible to take into account individually the nature of the contrast agent, the size of the syringe, the volume per minute of the injection and the stress to the patient.

Examples

For Levovist™ 200 mg/ml ultrasound contrast fluid, which is manufactured by Schering AG of Berlin, Germany, phase separation occurs within a couple of minutes (approximately 3-5 minutes) after preparation. This phase separation is characterized by contrast particles aggregating at the lower part of a syringe containing the contrast fluid and the watery diluent collecting above the contrast particles within the syringe.

A number of technical approaches to mitigating and/or preventing Levovist™ phase separation were tested using a standardized laboratory model. In the first technical approach, a small ferromagnetic ball (having a higher specific weight then Levovist™) was placed in a syringe and moved therein by means of a magnetic field applied thereto. In the second technical approach, an agitation element (having a higher specific weight then Levovist™) was placed in the syringe and moved therein by means of an external magnetic bar moved outside of and relative to the syringe.

Test Setup

The tests were conducted using in-vitro test equipment validated to simulate in-vivo contrast enhancement conditions. The test equipment allowed reproducible measurements of the enhancement characteristics of ultrasound contrast fluid suspensions.

Through the controlled movement or control of a magnetic field source, agitation elements placed in the syringe were able to be moved in a controlled fashion to agitate the ultrasound contrast fluid to prevent phase separation. After agitation, the ultrasound contrast fluid was injected into the testing equipment using a transfer tube and a 22G needle. The simulated body temperature was 37°C and the simulated negative pressure of the lung simulating component (i.e., oxygenator) of the testing equipment was 100 mBar.

Testing Method

Respective measurements of the enhancement properties of the ultrasound contrast fluid suspension over a prolonged period of time (up to 22 minutes) were conducted for syringes having magnetic agitation elements and for syringes not

incorporating magnetic agitation elements. A standard infusion / injection speed of 1 ml/min was used throughout the tests. The impact of the phase separation mitigation approaches were deducted from the variances in the measured Doppler-signal intensity.

Results – Test One

As shown in Figure 3, no agitation of the ultrasound contrast fluid suspension leads to significant unfavorable inconsistencies in the enhancement properties of the contrast fluid, which is not suitable for clinical applications. However, when a magnetic bar was used to agitate the ultrasound contrast fluid suspension within the syringe, by means of a magnetic source located outside of the syringe, the contrast fluid was resuspended and a long-lasting, stable enhancement pattern was achieved.

Results – Test Two

In this test, a ferromagnetic ball was moved within the syringe through application of an outside magnetic field. Again, as shown in Figure 4, the test results clearly indicate that resuspension of the ultrasound contrast fluid suspension leads to significantly more consistent enhancement properties when compared to non-resuspended ultrasound contrast fluid suspension. With regard to the non-resuspended contrast fluid enhancement properties, the differences compared to Results – Test One (above) show that the extent and impact of phase separation on contrast enhancement is largely unpredictable.

Results – Test Three

In this test, a magnetic bar was moved within the syringe through application of a ferromagnetic object outside the syringe. Besides a baseline comparison (i.e., compared to no resuspension of contrast fluid suspension), the influence of variations in the strength of the mechanical forces for resuspension were investigated. As can be clearly deducted from the test results, as shown in Figure 5, ultrasound contrast fluid suspensions contain fragile particles and the mechanical forces applied for resuspension must therefore be adjusted to the stability and strength of the contrast fluid suspension. An extremely vigorous resuspension is detrimental for

the enhancement properties of the contrast fluid, whereas a slight agitation may not prevent phase separation. The key is to adjust the resuspension mode in way that the forces impacting the contrast fluid particles do not impair or limit their contrast enhancement purpose. The level of mechanical force required and/or tolerable for each individual ultrasound contrast fluid, including Levovist™ varies, but a reproducible and controllable resuspension mode is required.

It should be appreciated that the present invention may be configured as appropriate for the application. The embodiments and example described above are to be considered in all respects only as illustrative and not restrictive. The scope of the invention is indicated by the following claims, rather than by the foregoing description. All changes which fall within the meaning and range of equivalency of the claims are to be embraced within their scope.

List of reference numerals:

1. Syringe
2. Plunger
3. Needle attachment
4. Holder
5. Injector
6. Ram
7. Motor
8. Ring
9. Magnet
10. Linkage
11. Collar
12. Thrust motor
13. Control device
14. Bulge
15. Ball
16. Coils
17. Magnetic collar
18. Control unit
20. Plunger bulge

WHAT IS CLAIMED IS:

1. A syringe for use with an injector, comprising:

a body comprising a distal discharge end;

a plunger movably disposed within the body; and

at least one agitation element disposed within the body between the plunger and the distal discharge end, the at least one agitation element operable to be acted on by a magnetic field to agitate the contents of the syringe, the magnetic field being generated by a source operably associated with at least one of the syringe and the injector.

2. The syringe of Claim 1 wherein the contents of the syringe comprise a contrast agent.

3. The syringe of Claim 2 wherein the contrast agent comprises an ultrasound contrast agent.

4. The syringe of Claim 1 wherein the at least one agitation element comprises a ferromagnetic or magnetic element.

5. The syringe of Claim 1 wherein the source comprises an electromagnetic field source.

6. The syringe of Claim 5 wherein the source comprises one or more coils operably associated with the syringe.

7. The syringe of Claim 1 wherein the source is operably associated with the injector and is moved mechanically outside the syringe.

8. The syringe of Claim 7 wherein the source comprises a magnet or a ferromagnetic element.

9. The syringe of Claim 1 wherein the at least one agitation element comprises a casing.

10. The syringe of Claim 1, further comprising a recess defined in the body of the syringe, the recess operable to accommodate the at least one agitation element.

11. The syringe of Claim 10 wherein the recess is defined adjacent to the distal discharge end of the syringe.

12. The syringe of Claim 1, further comprising a recess defined in the plunger of the syringe, the recess operable to accommodate the at least one agitation element.

13. The syringe of Claims 10-12 wherein the recess comprises an annular recess.

14. An injector system comprising:

an injector comprising means for mounting a syringe thereon;

a syringe comprising a body having a distal discharge end and means cooperable with the injector means for mounting the syringe on the injector, a plunger movably disposed within the body, and at least one agitation element disposed within the body between the plunger and the distal discharge end; and

a field source operably associated with at least one of the syringe and injector, the field source operable to generate a magnetic field that acts on the at least one agitation element to agitate the contents of the syringe.

15. The injector system of Claim 14 wherein the contents of the syringe comprise a contrast agent.

16. The injector system of Claim 15 wherein the contrast agent comprises an ultrasound contrast agent.

17. The injector system of Claim 14 wherein the at least one agitation element comprises a ferromagnetic or magnetic element.

18. The injector system of Claim 14 wherein the field source comprises an electromagnetic field source.

19. The injector system of Claim 18 wherein the field source comprises one or more coils operably associated with the syringe.

20. The injector system of Claim 14 wherein the field source is operably associated with the injector and is moved mechanically outside the syringe.

21. The injector system of Claim 20 wherein the field source comprises a magnet or a ferromagnetic element.

22. The injector system of Claim 14, further comprising a recess defined in the body of the syringe, the recess operable to accommodate the at least one agitation element.

23. The injector system of Claim 22 wherein the recess is defined adjacent to the distal discharge end of the syringe.

24. The injector system of Claim 14, further comprising a recess defined in the plunger of the syringe, the recess operable to accommodate the at least one agitation element.

25. The injector system of Claims 22-24 wherein the recess comprises an annular recess.

26. A method for agitating the contents of a syringe, comprising:

providing an injector comprising means for mounting a syringe thereon;

providing a syringe comprising a body having a distal discharge end and means cooperable with the injector means for mounting the syringe on the injector, a plunger movably disposed within the body, and at least one agitation element disposed within the body between the plunger and the distal discharge end;

providing a field source operably associated with at least one of the syringe and injector, the field source operable to generate a magnetic field that acts on the at least one agitation element to agitate the contents of the syringe;

activating the field source to generate the magnetic field;

applying the magnetic field to the at least one agitation element in the syringe; and

agitating the contents of the syringe with the at least one agitation element.

27. The method of Claim 26, further comprising:

deactivating the field source to terminate the agitation of the syringe contents.

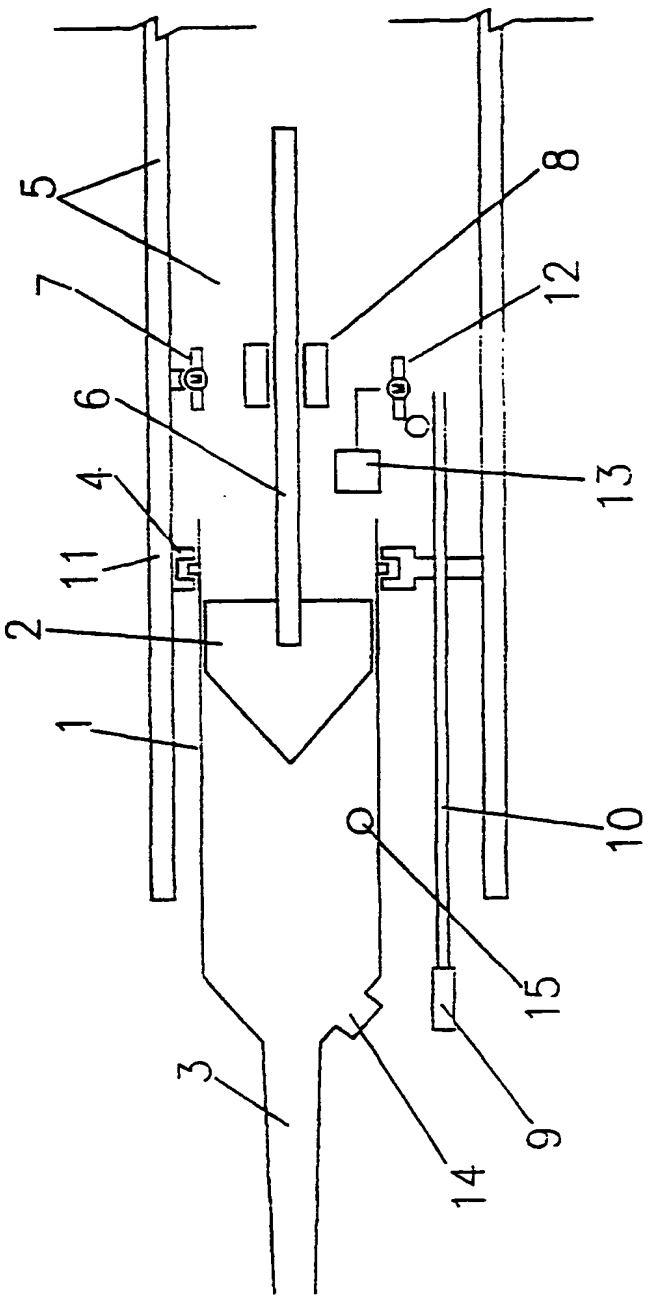


Figure 1

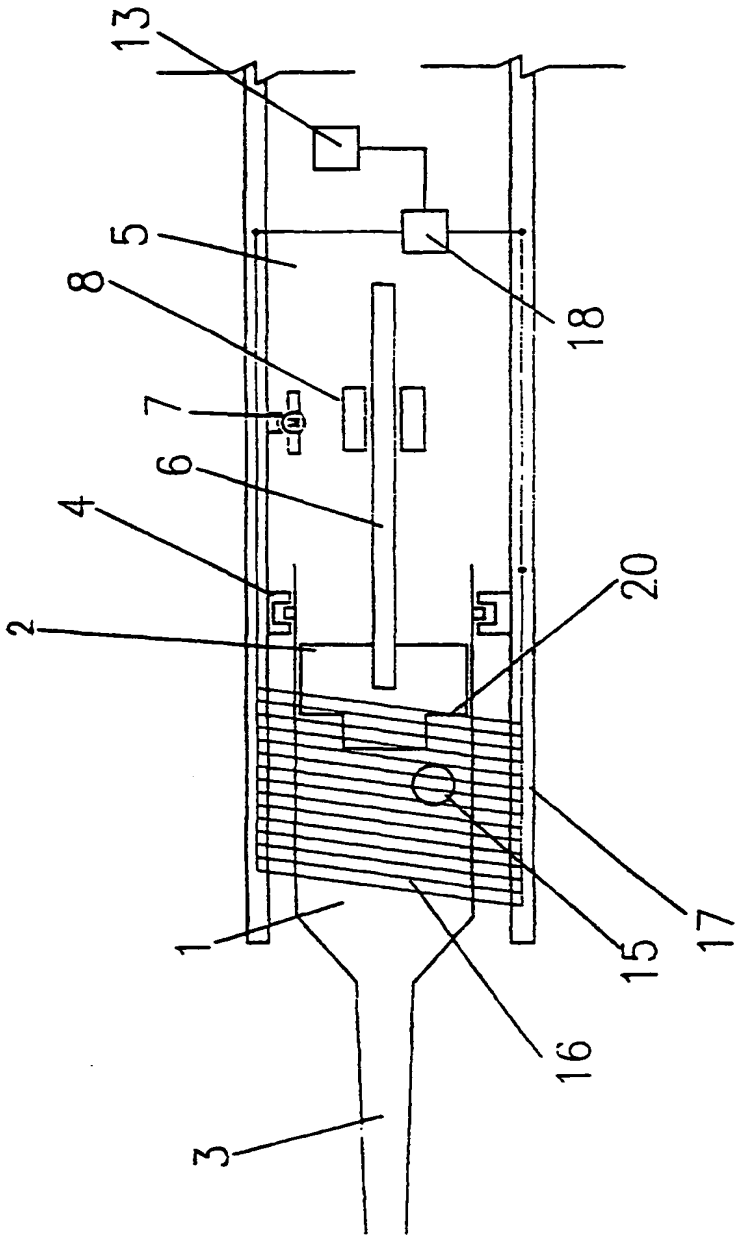


Figure 2

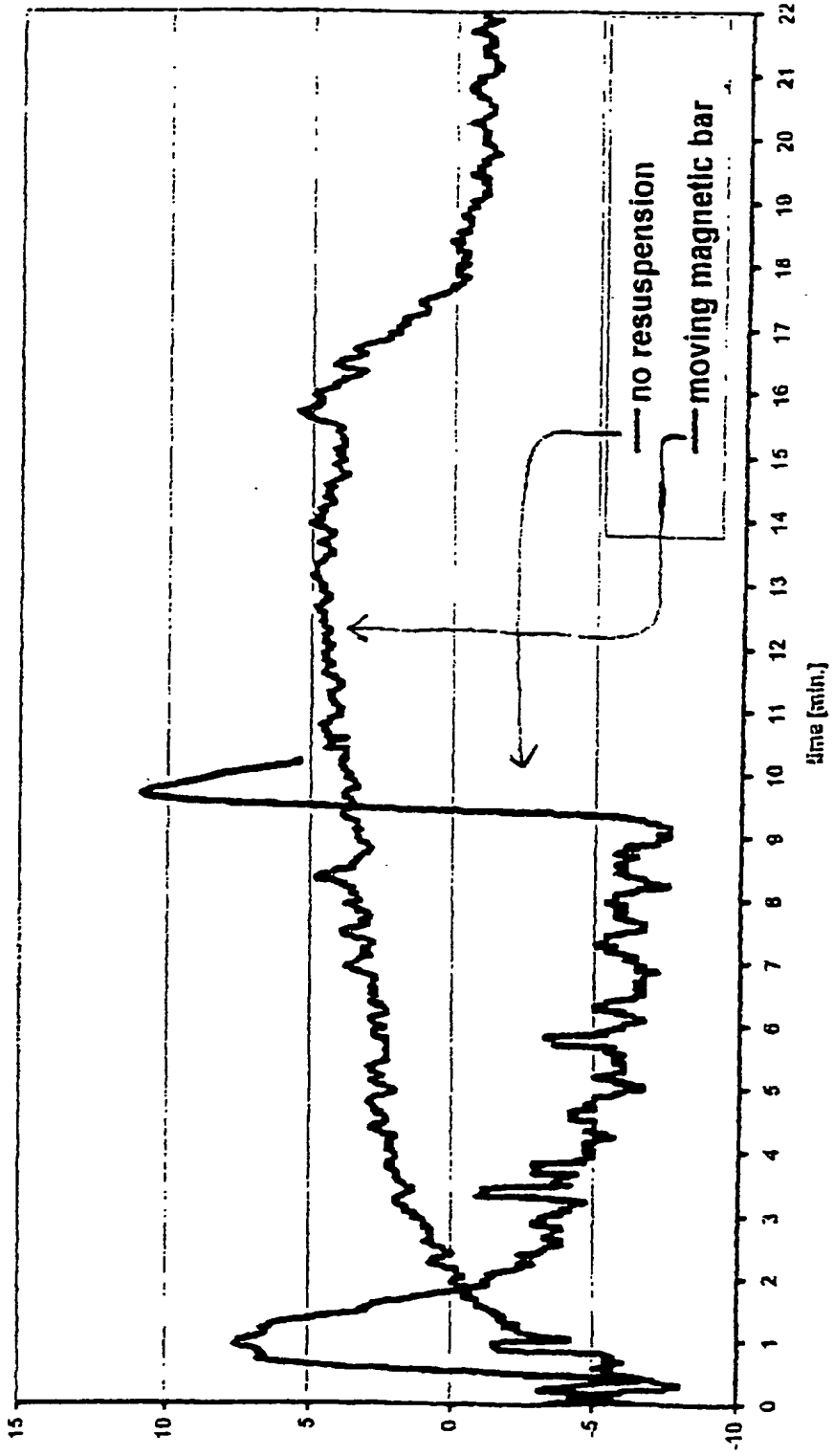

no resuspension
moving magnetic bar
Doppler intensity [dB]
time [min.]
15
10
5
0
-5
-10
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22

figure 3

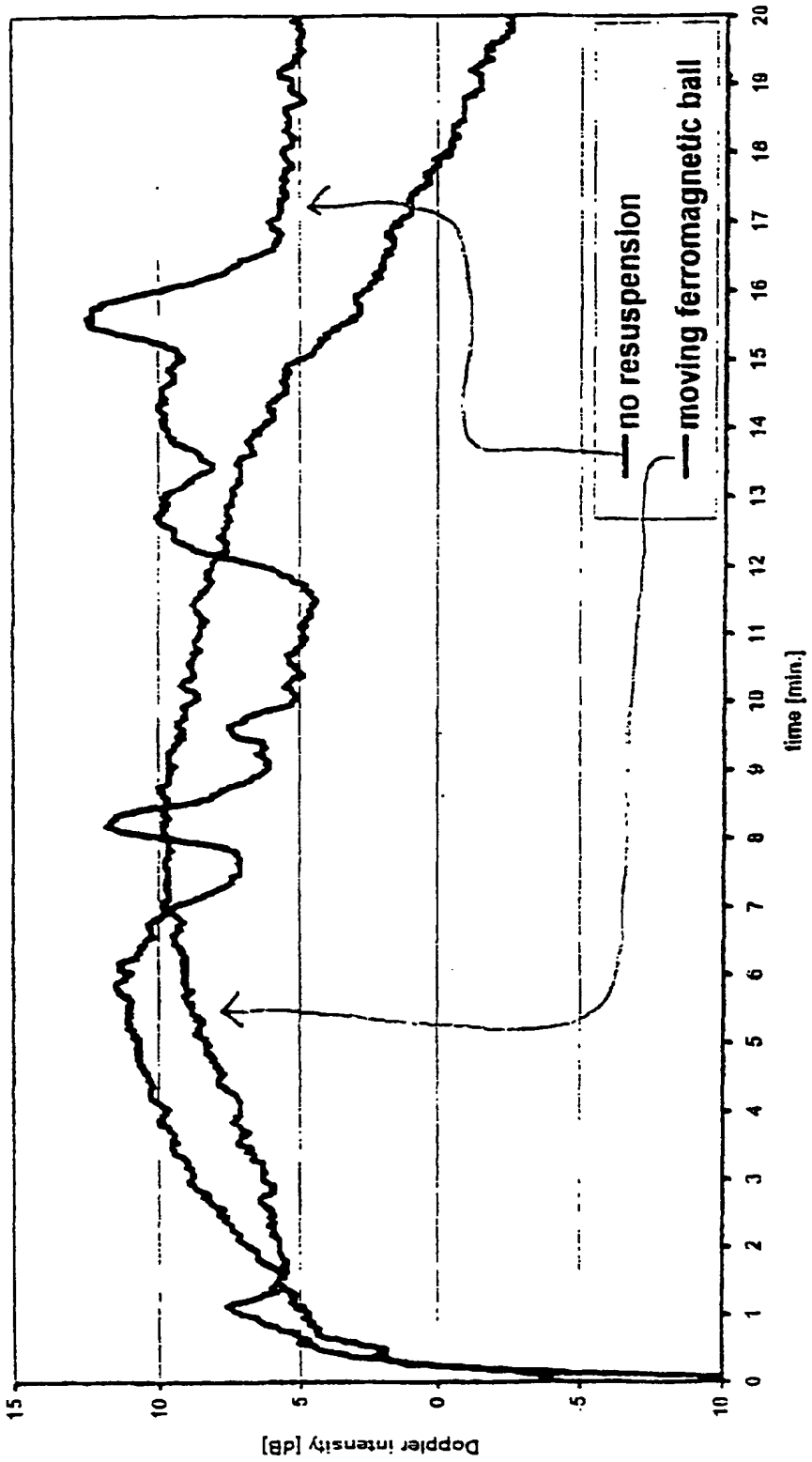

no resuspension
moving ferromagnetic ball
time [min.]
Doppler intensity [dB]
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
15
10
5
0
-5
-10

Figure 4

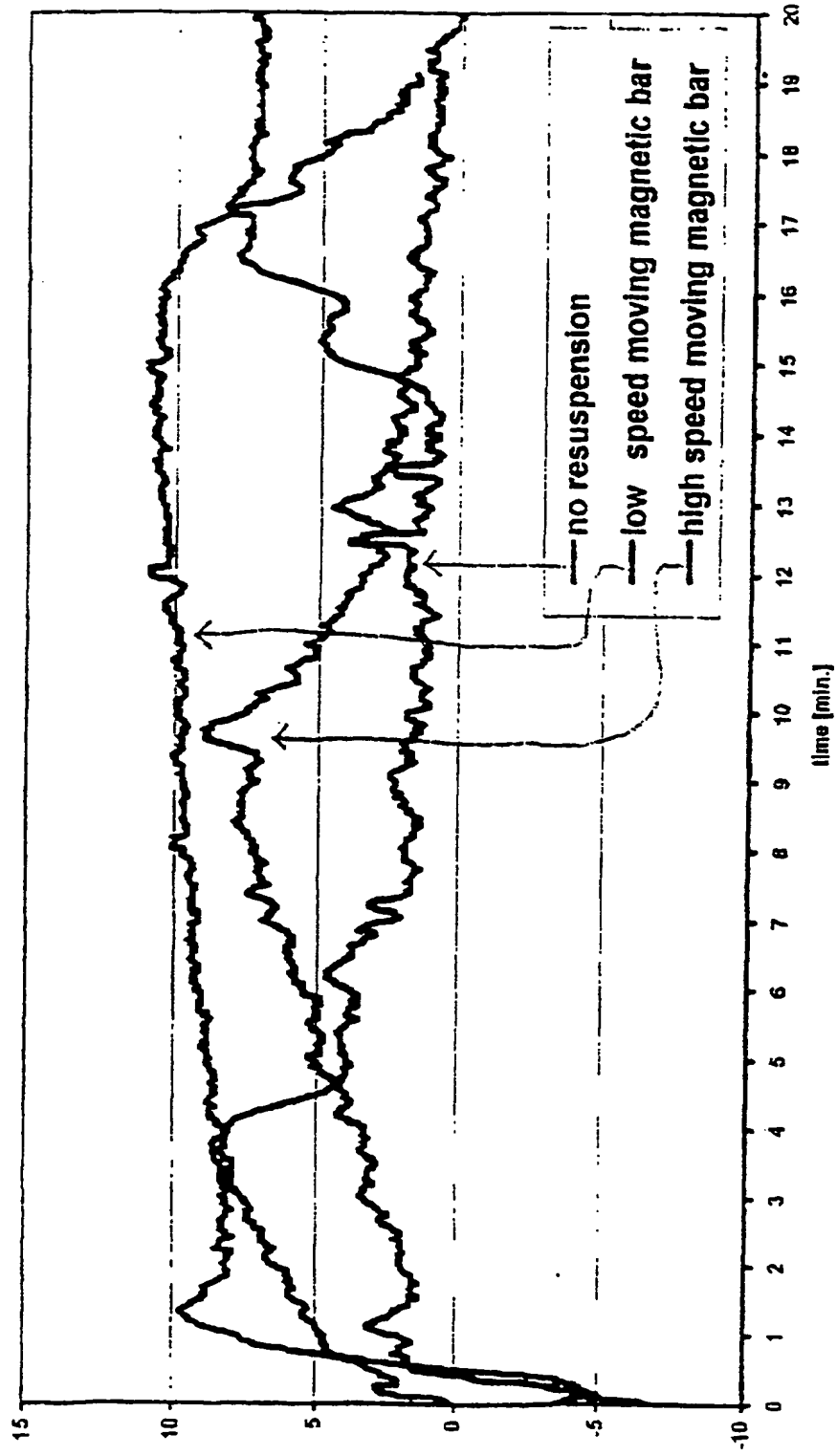

no resuspension
low speed moving magnetic bar
high speed moving magnetic bar
Doppler intensity [dB]
time [min.]
15
10
5
0
-5
-10
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20

figure 5

INTERNATIONAL SEARCH REPORT

Int dional Application No
PCT/EP 99/06289

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M5/145 B01F13/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M B01F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 296 22 313 U (TRICUMED GMBH) 6 March 1997 (1997-03-06) the whole document	1-27
X	US 5 352 036 A (HABER TERRY M ET AL) 4 October 1994 (1994-10-04) claims 1,5; figures	1,4-6, 9-11
X	US 5 240 322 A (HABER TERRY M ET AL) 31 August 1993 (1993-08-31) the whole document	1,4,9, 12,13
X	DE 39 34 024 A (WILDANGER HANS JOERG) 18 April 1991 (1991-04-18) the whole document	1,4,9, 14,17, 26,27

-/—

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 December 1999	11/01/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Clarkson, P

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/EP 99/06289

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 789 670 A (ROSENWALD G) 5 February 1974 (1974-02-05) column 3, line 27 -column 34; figures	1,4-14, 17-27

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 99/06289

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
DE 29622313	U	06-03-1997	NONE	
US 5352036	A	04-10-1994	NONE	
US 5240322	A	31-08-1993	NONE	
DE 3934024	A	18-04-1991	NONE	
US 3789670	A	05-02-1974	NONE	